

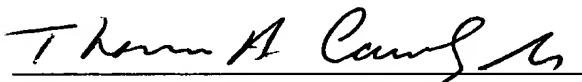
REMARKS

By the foregoing amendment, the applicants have introduced an amendment to the specification as it was amended during the international phase [see "Translation Of Amendment to the Specification of Intl. Appl. No. PCT/JP99/03682 as amended under PCT Article 34 (Translation of the Annex)" submitted to the USPTO on 27 February 2001].

The foregoing amendments to the claims correct obvious errors and more clearly define the applicants' invention. Support for new claims 44-46 is found throughout the specification and claims as originally filed. No new matter is believed to have been added.

Respectfully submitted,

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**APPENDIX A-SPECIFICATION
VERSION WITH MARKINGS TO INDICATE CHANGES MADE**

The paragraph beginning at page 11, line 17, was amended as follows.

--The location where the nucleic acid sequence for enhancing expression of a useful gene is incorporated into a gene expression vector [is not particularly limited as long as direct or indirect enhancement of expression of a useful gene is permitted] should be the one that permit direct or indirect enhancement of expression of a useful gene by means of incorporating the nucleic acid sequence for enhancing expression of a useful gene into an expression vector which has been constructed such that the useful gene can be expressed, however, it is preferable that the location is downstream of the expression regulatory promoter sequence and upstream of the useful gene. Additionally, the nucleic acid sequence for enhancing expression of a first useful gene should be incorporated into the expression vector such that transcription and translation are carried out in the normal (i.e., from 5' to 3') direction.--

APPENDIX A-CLAIMS

VERSION WITH MARKINGS TO INDICATE CHANGES MADE

Please amend claims 1 and 14-18 as follows.

1. (Amended) A nucleic acid sequence for enhancing expression of a useful gene incorporated into a gene expression vector for enhancing expression of a useful gene comprising a nucleic acid sequence corresponding to a 5'-untranslated region of a viral gene or a fragment or a variant thereof, and is incorporated downstream of the expression regulatory promoter sequence and upstream of the first useful gene in a gene expression vector.

14. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim 12, wherein said nucleic acid sequence consists of [the following nucleotide sequence: gccagccccc tgatgggggc gacactccac catagatcac tcccctgtga ggaactactg 60 tcttcacgca gaaagcgtct agccatggcg ttagtatgag tgcgtgcag cctccaggac 120 cccccctccc gggagagcca tagtggtctg cggaaccggt gactacaccg gaattgccag 180 (SEQ ID NO: 1, 1-180)] nucleotides 1-180 of SEQ ID NO: 1.

15. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim 12, wherein said nucleic acid sequence consists of [the following nucleotide sequence: gacgaccggg tcctttcttg gatcaaccgc ctcaatgcct ggagatttgg gcgtgcccc 60 gcgagactgc tagccgagta gtgtgggtc gcgaaaggcc ttgtgttact gcctgatagg 120 gtgcttgca gtgccccggg aggtctcgta gaccgtgcac c 161 (SEQ ID NO: 1, 181-341)] nucleotides 181-341 of SEQ ID NO: 1.

16. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim 12, wherein said nucleic acid sequence consists of [the following nucleotide sequence:

gccagccccc tgatgggggc gacactccac catagatcac tcccctgtga ggaactactg 60
tcttcacgca gaaagcgtct agccatggcg ttagtatgag tgcgtgcag cctccaggac 120
ccccctccc gggagagcca tagtggtctg cggaaccggt gactacaccg gaattgccag 180
gacgaccggg tcctttcttg gatcaaccgc ctcaatgcct ggagatttgg gcgtgcccc 240
gcgagactgc tagccgagta gtgtgggtc gcgaaaggcc ttgtgttact gcctgatagg 300

gtgcttgca gtgccccggg aggtctcgta gaccgtgcac c 341

(SEQ ID NO: 1, 1-341)] nucleotides 1-341 of SEQ ID NO:1.

17. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim 13, wherein said nucleic acid sequence consists of [the following nucleotide sequence:

gacgaccggg tcctttcttg gatcaacccg ctcaatgcct ggagatttgg gcgtgcccc 60
gcgagactgc tagccgagta gtgttgggtc gcgaaaggcc ttgtgttact gcctgatagg 120
gtgcttgca gtgccccggg aggtctcgta gaccgtgcac catgagcaca aatcctaaac 180
ctcaaagaaa aaccaaactg aacaccaacc gccgcccaca ggacgtcaag tccccgggcg 240
gtggtcagat cgttgggtga gtttacctgt tgccgcgcag gggccccagg ttgggtgtgc 300
gcgcgactag gaagacttcc gagcggtcgc aacctcgtgg aaggcgacaa cctatcccca 360
aggctcgccg gcccgagggc aggacctggg ctacgcccgg gtatccttgg cccctctatg 420
gcaacgaggg catgggggtg gcaggatggc tcctgtcgcc ccgcggtcc cggcctagtt 480
ggggcccttc ggacccccgg cgtaggtcgc gtaatttggg taaggtcatc gat 533

(SEQ ID NO: 1, 181-713)] nucleotides 181-713 of SEQ ID NO: 1.

18. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim 13, wherein said nucleic acid sequence consists of [the following nucleotide sequence:

gccagcccc tgatgggggc gacactccac catagatcac tcccctgtga ggaactactg 60
tcttcacga gaaagcgtct agccatggcg ttagtatgag tgcgtgcag cctccaggac 120
ccccctccc gggagagcca tagtggctcg cggaaccggt gactacaccg gaattgccag 180
gacgaccggg tcctttcttg gatcaacccg ctcaatgcct ggagatttgg gcgtgcccc 240
gcgagactgc tagccgagta gtgttgggtc gcgaaaggcc ttgtgttact gcctgatagg 300
gtgcttgca gtgccccggg aggtctcgta gaccgtgcac catgagcaca aatcctaaac 360
ctcaaagaaa aaccaaactg aacaccaacc gccgcccaca ggacgtcaag tccccgggcg 420
gtggtcagat cgttgggtga gtttacctgt tgccgcgcag gggccccagg ttgggtgtgc 480
gcgcgactag gaagacttcc gagcggtcgc aacctcgtgg aaggcgacaa cctatcccca 540
aggctcgccg gcccgagggc aggacctggg ctacgcccgg gtatccttgg cccctctatg 600
gcaacgaggg catgggggtg gcaggatggc tcctgtcgcc ccgcggtcc cggcctagtt 660

ggggcccttc ggacccccgg cgtaggtcgc gtaatttggg taaggtcatc gat 713
(SEQ ID NO: 1, 1-713)] nucleotides 1-713 of SEQ ID NO:1.

Claim 19 was canceled, without prejudice.

Claims 21-28, 35, and 37-40 were amended as follows.

21. (Amended) [The] A nucleic acid sequence for enhancing expression of a useful gene [according to claim 15,] wherein said nucleic acid has] incorporated into a gene expression vector for enhancing expression of a useful gene comprising a nucleic acid sequence of nucleotides 181-341 of SEQ ID NO: 1 having one thymidine inserted into position 207 of SEQ ID NO: 1, and a fragment or variant thereof.

22. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim 1 or claim 21, wherein said nucleic acid sequence for enhancing expression of a useful gene enhances expression of a useful gene by means of its own translation promoting activity.

23. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim 1 or claim 21, wherein said nucleic acid sequence for enhancing expression of a useful gene enhances expression of a useful gene by means of accelerating IRES activity.

24. (Amended) A nucleic acid sequence for enhancing expression of a useful gene comprising [the following] a nucleotide sequence[:

gccagccccc tgatgggggc gacactccac catagatcac tcccctgtga ggaactactg 60
tcttcacgca gaaagcgtct agccatggcg ttagtatgag tgcgtgcag cctccaggcc 120
ccccctccc gggagagcca tagtggtctg cggaaccggt gactacaccg gaattgccag 180
gacgaccggg tcctttcttg gatcaatccc gctcaatgcc tggagatttg ggcgtgcccc 240
cgcgagactg ctaggcgagt agtgttgggt cgcgaaaggc cttgtgttac tgcctgatag 300
ggtgcttgcg agtgccccgg gaggtctcgt agaccgtgca cc 342

(SEQ ID NO: 7)] of SEQ ID NO: 7, which enhances expression of a useful gene by means of

promoting mRNA translation in an IRES-dependent manner.

25. (Amended) A nucleic acid sequence for enhancing expression of a useful gene which comprises a polynucleotide having a similar IRES activity to an IRES activity of [the following] a nucleotide sequence[:

gccagccccc tgatgggggc gacctccac catagatcac tcccctgtga ggaactactg 60
tcttcacgca gaaagcgtct agccatggcg ttagtatgag tgcgtgcag cctccaggcc 120
ccccctccc gggagagcca tagtggtctg cggaaccggt gactacaccg gaattgccag 180
gacgaccggg tcctttcttg gatcaatccc gctcaatgcc tggagatttg ggcgtgcccc 240
cgcgagactg ctgcccaggt agtgttgggt cgcgaaaggc cttgtgttac tgcctgatag 300
ggtgcttgcg agtgccccgg gaggtctcgt agaccgtgca cc 342

(SEQ ID NO: 7)] of SEQ ID NO: 7, and consisting of a fragment or a variant of the sequence, which enhances expression of a useful gene by means of promoting mRNA translation in an IRES-dependent manner.

26. (Amended) An isolated polynucleotide consisting of [the following] a nucleotide sequence[:

gccagccccc tgatgggggc gacctccac catagatcac tcccctgtga ggaactactg 60
tcttcacgca gaaagcgtct agccatggcg ttagtatgag tgcgtgcag cctccaggcc 120
ccccctccc gggagagcca tagtggtctg cggaaccggt gactacaccg gaattgccag 180
gacgaccggg tcctttcttg gatcaatccc gctcaatgcc tggagatttg ggcgtgcccc 240
cgcgagactg ctgcccaggt agtgttgggt cgcgaaaggc cttgtgttac tgcctgatag 300
ggtgcttgcg agtgccccgg gaggtctcgt agaccgtgca cc 342

(SEQ ID NO. 7)] of SEQ ID NO:7.

27. (Amended) An isolated polynucleotide having a similar IRES activity to an IRES activity of [the following] a nucleotide sequence[:

gccagccccc tgatgggggc gacctccac catagatcac tcccctgtga ggaactactg 60
tcttcacgca gaaagcgtct agccatggcg ttagtatgag tgcgtgcag cctccaggcc 120
ccccctccc gggagagcca tagtggtctg cggaaccggt gactacaccg gaattgccag 180
gacgaccggg tcctttcttg gatcaatccc gctcaatgcc tggagatttg ggcgtgcccc 240

cgcgagactg ctagccgagt agtgttgggt cgcgaaaggc cttgtgttac tgcctgatag 300

ggtgcttgcg agtgccccgg gaggtctcgt agaccgtgca cc 342

(SEQ ID NO: 7)], of SEQ ID NO: 7 and consisting of a fragment or a variant of said sequence.

28. (Amended) A gene expression vector comprising the nucleic acid sequence for enhancing expression of a useful gene according to claim 1 or claim 21.

35. (Amended) A therapeutic composition for treating diseases resulting from reduction of cap-dependent mRNA translation in a body of organisms, comprising the nucleic acid sequence for enhancing expression of a useful gene according to claim 1 or claim 21 such that translation of mRNA can be promoted by means of introducing said nucleic acid sequence for enhancing expression of a useful gene into the body of the organisms.

37. (Amended) A method for determining the severity of hepatitis C, comprising the steps of: detecting the presence of a target polynucleotide sequence contained in a biological sample derived from a test subject, by using the polynucleotide according to claim 26 or claim 27 as the target; and determining the severity of the hepatitis C based on the presence of the sequence.

38. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim [16, wherein said nucleic acid has] 21 further comprising a nucleic acid sequence of nucleotides 1-180 of SEQ ID NO: 1 having one thymidine inserted into position 207 of SEQ ID NO: 1, and a fragment or variant thereof.

39. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim [17, wherein said nucleic acid has] 21 further comprising a nucleic acid of nucleotides 342-713 of SEQ ID NO: 1 having one thymidine inserted into position 207 of SEQ ID NO: 1, and a fragment or variant thereof.

40. (Amended) The nucleic acid sequence for enhancing expression of a useful gene according to claim [18, wherein said nucleic acid has] 21 further comprising a nucleic acid sequence of nucleotides 1-180 and 342-713 of SEQ ID NO: 1 having one thymidine inserted into position 207 of SEQ ID NO: 1, and a fragment or variant thereof.

New claims 44-46 were added herein.

44. The nucleic acid sequence for enhancing expression of a useful gene according to claim 1, wherein the 5'-untranslated region comprises a sequence corresponding to at least one region selected from the group consisting of a pyrimidine-rich tract, BoxA, BoxB, a trans factor-binding site, and a combination thereof.

45. The nucleic acid sequence for enhancing expression of a useful gene according to claim 44, wherein said nucleic acid comprises a sequence having substitution, deletion, insertion and/or addition of a single or a few nucleotides of a sequence derived from a wild-type virus within the sequence or a proximate sequence in at least one position corresponding to a pyrimidine-rich tract, BoxA, BoxB and/or trans factor-binding site contained in the 5'-untranslated region.

46. A therapeutic composition for treating diseases resulting from reduction of IRES activity in a body of organisms, comprising the nucleic acid sequence for enhancing expression of a useful gene according to claim 25 such that translation of mRNA can be promoted by means of introducing said nucleic acid sequence for enhancing expression of a useful gene into the body of the organisms.